New claim 21 has been added directed to the specific subject matter that the Examiner indicates in the Office Action is fully enabled. Accordingly, newly-submitted claim 21 is not open to rejection under 35 USC 112, first paragraph, as lacking an enabling disclosure.

It is noted that claims 7 to 10 were not included in the rejection and hence it is assumed that these claims are considered to be fully enabled. With respect to claims 1 to 6, claim 1 has been limited to a strain of *Leishmania* as the macrohage infecting parasite and to the parasite being transformed with a plasmid containing the GM-CSF gene. Claims 2 and 7 have been cancelled consequentially. Claims 3, 5, 6 and 7 have been made dependent on claim 1 consequentially.

It is submitted that the exemplification contained in the specification, namely the construction of plasmids pneo-mGM CSF and pneo-hGM CSF, containing respectively the murine and human GM CSF genes, of known nucleic acid sequence, the neo gene flanked by the intergenic regions of the α- tubulin gene of *L. enriettii*, also of known nucleic acid sequence, and transformation of representative strains of *Leishmania*, namely *L. major* and *L. donovani*, and expression of the genes, provides sufficient enablement for the amended claims.

Accordingly, the rejection of claims 1 to 6 and 11 to 16, insofar as they remain in the application and in their amended form, cannot be considered open to rejection under 35 USC 112, first paragraph, and hence the rejection should be withdrawn.

The Examiner made several claim rejections:

- Claims 1 to 3 and 10 under 35 USC 102(b) as being anticipated by Moore et al
- Claims 5 to 6 under 35 USC 103(a) as being unpatentable over Moore et al in view of Wong et al
- Claims 7 to 8 under 35 USC 103(a) as being unpatentable over Moore et al in view of Wong et al and further in view of Laban et al.
- Claims 9 and 11 to 16 under 35 USC 103(a) as being unpatentable over Moore et al in view of Matlashewski et al

These claim rejections do not include rejection of claim 4. Each of these rejections is based on the Moore et al reference. The rejections are founded on the incorrect premise that:

> "Moore et al disclose a macrophage infecting parasite such as Leishmania expressing a granulocyte macrophage colony stimulating factor (GM-CSF) and additional cytokine e.g., IL-6 ..."

It is submitted that this is an entirely incorrect characterization of the reference. The Moore et al reference is concerned with the effect of a strain of *Leishmania* (*L. donovani*) promastigotes upon infection of bone-marrow macrophages (BMMs). An observation of the author is that infection of BMMs by *L. donovani* caused cytokine gene expression by the BMMs. The cytokine gene expression, including the gene for GM-CSF, is from the BMMs. It is stated on page 2934:

> "It is interesting that although *L. donovani* infected BMMs express the GM-CSF gene, we were unable to detect GM-CSF protein in supernatants from infected cells".

Moore et al does not disclose or suggest any macrophage infecting parasite which is modified to express GM-CSF.

In the present application, applicant's claims are directed to a macrophage infecting parasite which is a strain of *Leishmania*, which is modified to express GM-CSF. It is the strain itself which is modified herein, so as to provide expression from the strain of GM-CSF.

To emphasize the distinction over the art, claim 1 has been amended, as discussed above, to recite that the *Leishmania* strain has been transformed by a plasmid containing the GM-CSF gene. It is submitted that the parasite claimed herein is something quite different from the disclosure of Moore et al, where the *Leishmania* is not transformed or otherwise modified.

The secondary references are not relied on for any basic modification of the teachings of Moore et al with respect to modification of the parasite. In particular, the secondary references are relied on as follows:

- Wong et al for a teaching of the human and murine GM-CSF gene
- Laban et al for a teaching of the expression of the neomycin gene using the α-tubulin intergenic sequences of *L. enriettii*
- Matlashewski et al for a teaching of differential expression of *Leishmania* gene and proteins that have utility as vaccines, as diagnostic reagents and for the generation of immunological reagents and the generation of attenuated variants of *Leishmania*.

All the above technical content of the secondary references in combination with the teachings of Moore et al in no manner suggests transformation of a strain of *Leishmania* by a plasmid containing a GM-CSF gene, as required by applicant's claims.

Accordingly, it is submitted that:

- Rejection of claims 1 to 7 and 10 under 35 USC 102(b) as being anticipated by Moore et al
- Rejection of claims 5 to 6 under 35 USC 103(a) as being unpatentable over Moore et al in view of Wong et al
- Rejection of claims 7 to 8 under 35 USC 103(a) as being unpatentable over Moore et al in view of Wong et al and Laban et al
- Rejection of claims 9 and 11 to 16 under 35 USC 103(a) as being unpatentable over Moore et al in view of Matlashewski et al

insofar as they remain in the application and in their amended form, should be withdrawn.

The Examiner rejected claims 1 to 6 and 10 under 35 USC 101 as being directed to a naturally-occurring macrophage infecting parasite expressing a GM-CSF gene and cytokine which is a product of nature. Since naturally-occurring *Leishmania* do not express cytokines, including GM-CSF, the source of the Examiner's rejection is unclear and the Examiner does not elaborate as to the potential source of his rejection.

In any event, it is noted that claim 1 now specifically recites that the *Leishmania* strain is transformed with the recited plasmid and hence claim 1 clearly refers to a *Leishmania* strain which has been genetically modified and hence cannot be considered to be a "product of nature".

Accordingly, the rejection of claims 1 to 6 and 10, insofar as they remain the application and in their amended form, as being directed to non-statutory subject matter, should be withdrawn.

The Examiner provisionally rejected claims 1 to 16 under 35 USC 101 as claiming the same invention as that of claims 1 to 16 of copending Application No. 08/713,768. As the Examiner notes, the rejection is a provisional one, since the conflicting claims have not in fact been patented.

It will be noted that claims 11 to 20 have been deleted from this application and in copending Application No. 08/713,768, claims 11 to 20 are being prosecuted and claims 1 to 10 have been deleted. In view of the mutual exclusivity of the claimed subject matter, it is submitted that there is no same invention double patenting rejection, provisional or otherwise. The rejection should be withdrawn.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,

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